Joint and muscle pain in Systemic Lupus Erythematosus

Associate prof shereen algergawy-
rheumatology and rehabilitation
Benha faculty of medicine

Systemic Lupus Erythematosus

Autoimmune disorder affecting multiple organ systems characterized by the production of autoantibodies”

Systemic Lupus Erythematosus

Prevalence:

- Almost 90% of all cases occur in women
- Overall, SLE affects women eight times more often than it does men
- At age 30 years, the ratio of women to men is 10:1
- The ratio at age 65 years, the ratio appears to be about 3:1
- The prevalence rate among women between ages 15 and 64 years is 1 in 700 women
- Symptoms usually appear between ages 15 and 25 years
- The prevalence in the general population is about 1 in 1000

Racial predisposition:

x 3 more common in blacks

Epidemiology in the young and elderly

- **Peak incidence is at age 15-40**

  But: Onset may be at any age

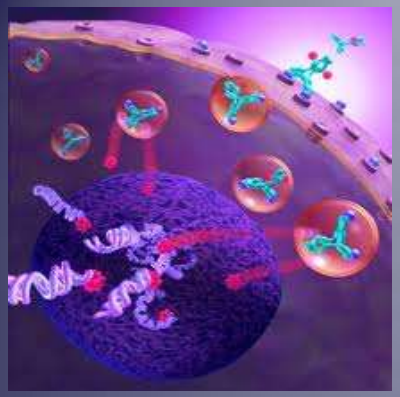
- **<u>In pre-pubertal and post menopausal</u>:**
  female : male ratio 3:1

Systemic Lupus Erythematosus

Etiology:

- **The etiology of SLE is currently unknown, but there are environmental and genetic factors involved**
- **Environmental Factors: Ultraviolet light (UVB), Alfalfa sprouts, chemicals (hydrazines) ? Drugs (Resprim = Trimethoprim + sulphamethoxazole), Infections (parvovirus, CMV, HCV), Smoking**
- **B cell activation results in increased autoantibody (mainly IgG) production to a variety (up to 2000) of antigens (nuclear, cytoplasmic and plasma membrane), e.g. ANA, anti-dsDNA.**
- **Development of and failure to remove immune complexes from the circulation leads to deposition of complexes in the tissue, causing vasculitis and disease (e.g. glomerulonephritis). Immune complexes also from in situ, e.g. kidney glomerular basement membrane**.
- There is impaired T cell regulation of the immune response.

Petri, M., Lazaro, D. (2009). *Systemic Lupus Erythematosus: Physicians' Information & Education Resource* . Retrieved from *http://online.statref.com*



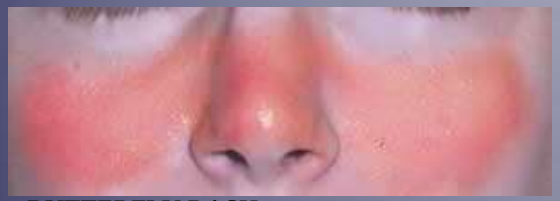
Systemic Lupus Erythematosus

Signs & Symptoms: PERCENTAGE (%)

- **Achy joints / arthralgia – 95%**
- **Fever of more than 100 degrees F / 38 degrees C - 90%**
- **Arthritis / swollen joints – 90%**
- **Prolonged or extreme fatigue – 81%**
- **Skin Rashes – 74%**
- **Anemia – 71%**
- **Kidney Involvement - 50%**
- **Pain in the chest on deep breathing / pleurisy – 45%**
- **Butterfly-shaped rash across the cheeks and nose - 42%**
- **Sun or light sensitivity / photosensitivity - 30%**
- **Hair loss / Alopecia - 27%**
- **Abnormal blood clotting problems – 20%**
- **Fingers turning white and/or blue in the cold – 17%**
- **Mouth or nose ulcers – 12%**

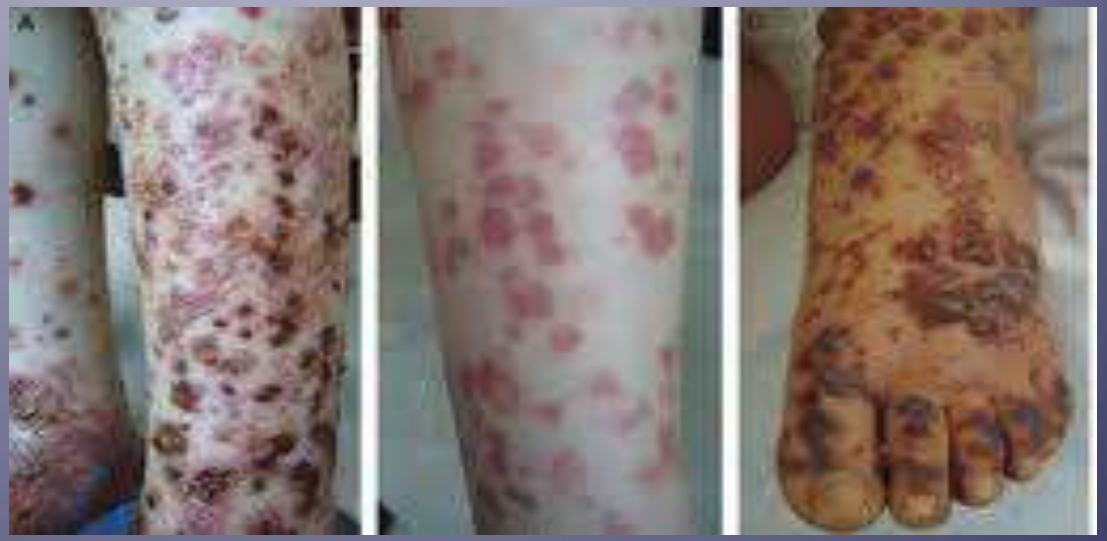
Petri, M., Lazaro, D. (2009). *Systemic Lupus Erythematosus: Physicians' Information & Education Resource* . Retrieved from *http://online.statref.com*

Systemic Lupus Erythematosus

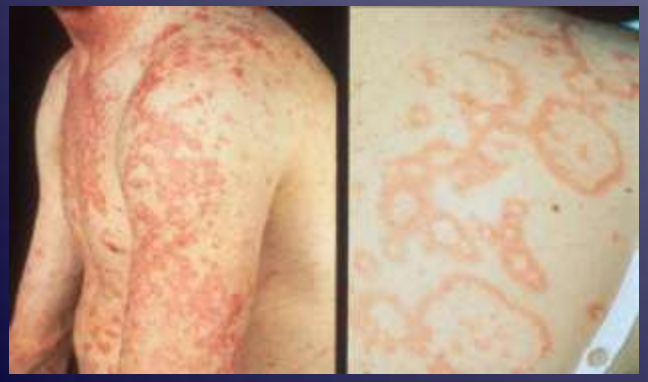


BUTTERFLY RASH

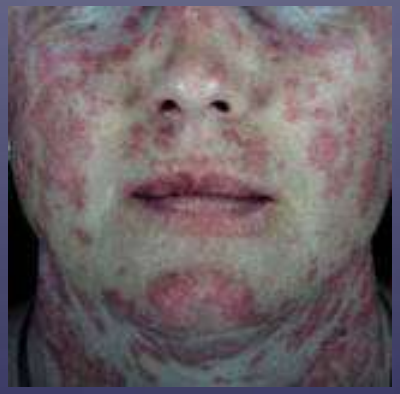
PHOTOSENSITIV
E ERYTHEMA



ERYTHMATOUS BULLOUS LESIONS

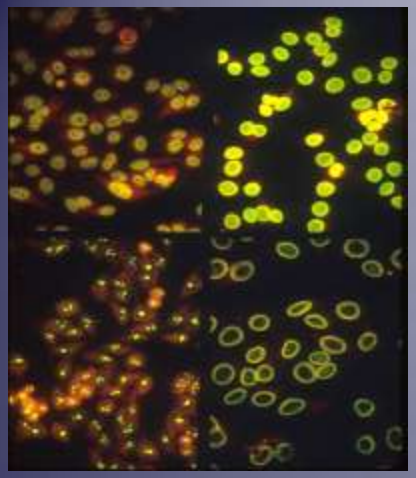


SUBACUTE CUTANEOUS
RASH



DISCOID LUPUS

Images : dermatlas.org



Systemic Lupus Erythematosus

Pathophysiology:

- The plasma cells are producing antibodies that are specific for self proteins, namely ds-DNA
- Overactive B-cells. Estrogen is a stimulator of B-cell activity
- Suppressed regulatory function in T-cells . Lack of T-cells
- IL-10, also a B-cell stimulator is in high concentration in lupus patient serum. High concentration linked to cell damage caused by inflammation
- Increased levels of Ca^{2+} . Leads to spontaneous apoptosis

ANAs in SLE

ANA's can be divided into:

- those directed against dsDNA
- those directed against ssDNA
- those directed against histones
- those directed against non-histone nuclear proteins : nucleic acid-protein complexes

ANAs in SLE

Autoantibody	Prevalence
anti- ds DNA	50-60%
anti- ss DNA	60-70%
anti- Histones	70%
anti- Sm (Smith)	30%
anti- RNP	35%
anti- Ro (SSA)	30%
anti- La (SSB)	15%

Anti DNA antibodies in SLE

- Anti ss- DNA:
  nonspecific and not in clinical use

- Anti-ds DNA: specific for SLE

  Clinical use important:
  - levels correlate with disease activity
  - presence and level associated with risk for renal disease
  - pathogenic effect mediated through direct binding to glomeruli or immune-complex mechanisms.

Clinical Associations of Auto-antibodies in SLE

ANTIBODY	FREQUENCY %	SPECIFICITY	CLINICAL SUBSET
dsDNA	50-60	++	Nephritis
ssDNA	60-70	-	
Histones	70	+	Drug-induced LE
Ro	30	+	Subactue
La	15	+	cutaneous Lupus, Heart block
Sm	30	++	Nephritis,CNS
RNP	10	+	MCTD
Antiphospholipid antibodies	30-40		Thrombosis Recurrent fetal loss

Diagnosis of SLE

- Based on a combination of clinical manifestations and laboratory findings which may occur simultaneously or serially

- Classification criteria are used for research

Classification criteria of SLE

- Criterion
- Malar Rash
- Discoid rash

- Photosensitivity
- Oral ulcers
- Arthritis
- Serositis
- Renal disorder

- Neurologic disorder
- Hematologic disorder

- Definition
- - Fixed erythema, malar distribution
- - Erythematous raised patches with
- scaling, atrophy, scarring
- - Skin rash as result of sunlight
- - Oral\ nasopharyngeal, usually painless
- - Nonerosive, 2 or more joints
- - Pleuritis OR Pericarditis
- -Proteinuria > 0.5gr or >+3 OR
- cellular casts
- - Seizures OR Psychosis

- - Hemolytic anemia OR
- Leukopenia < 4000/ mm3 OR
- Lymphopenia <1500/mm3 OR
- Thrombocytopenia < 100.000/mm3

Classification criteria of SLE

Criterion	Definition
10. Immunologic disorder	- anti-dsDNA OR - anti- Sm OR - false positive VDRL / anti-phospholipid antibody
11. Anti-nuclear antibody	Abnormal titer of ANA in absence of drugs known to cause DIL

Joint and Muscle Pain in Systemic Lupus Erythematosus (SLE)

More than 90 percent of people with SLE will experience joint and/or muscle pain at some time during the course of their illness. At the onset of the disease, the major complaint of more than half of SLE patients is pain in the joints.
The major cause of joint pain in SLE is inflammation of the joints. The term for this is arthritis. In the affected joint, arthritis can cause:

- pain
- swelling
- tenderness
- a feeling of warmth
- fluid collection.

- Pain in and around the joints is not always due to lupus arthritis. It also can be due to other medical disorders that may complicate or co-exist with SLE, including:

. fibromyalgia

. avascular necrosis of bone

. bursitis and tendonitis,

. other types of arthritis

. infection.

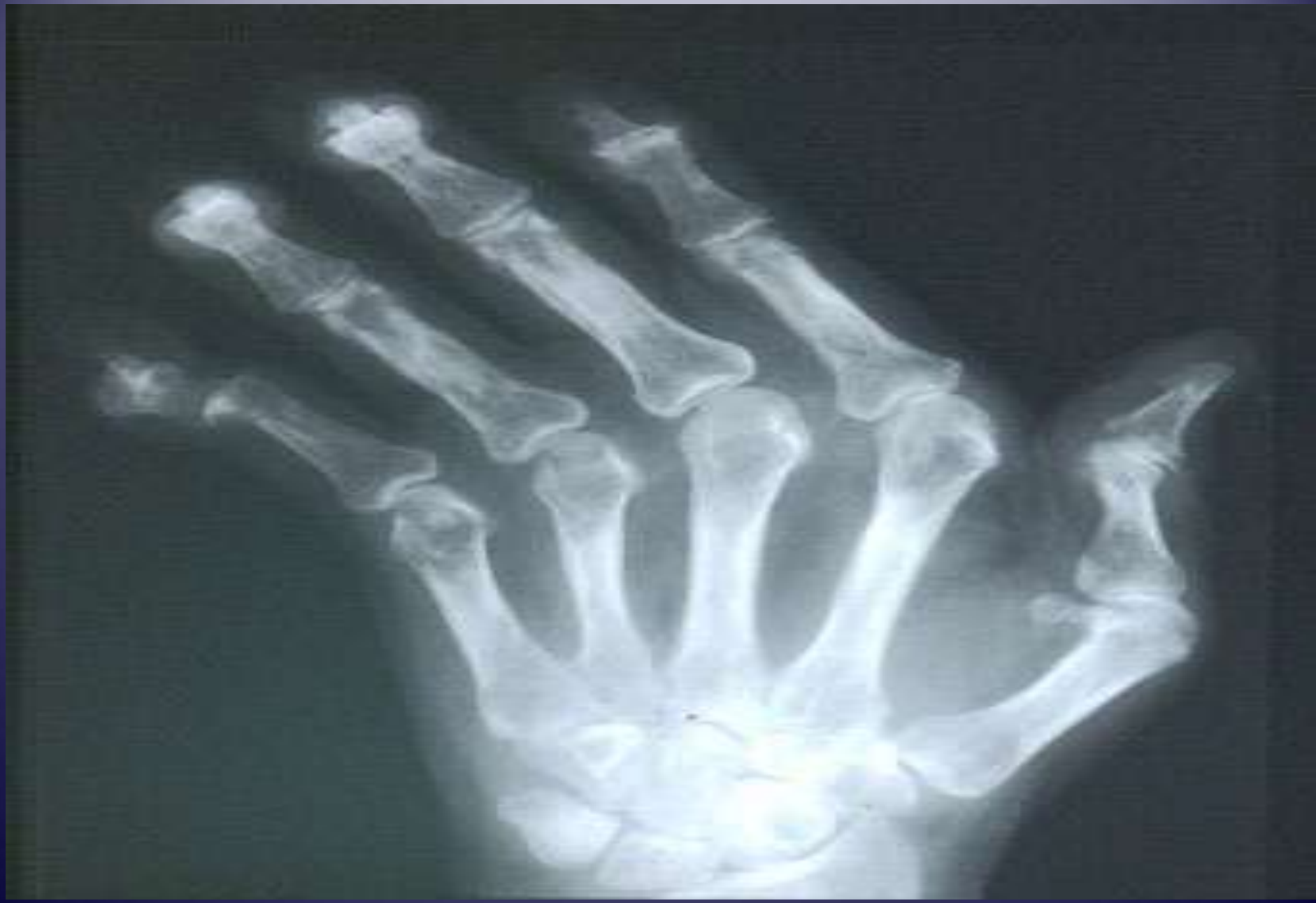
Lupus Arthritis

Lupus arthritis causes pain, stiffness, swelling, tenderness, and warmth of joints, and several joints are involved at one time. Joints farthest from the trunk of the body are affected most commonly, such as :

- **fingers**
- **wrists**
- **elbows**
- **knees**
- **ankles**
- **toes**

- The inflammation is symmetrical in distribution, which means it affects similar joints on both sides of the body.
- Generalized stiffness that occurs upon awakening in the morning will gradually improve as the day goes on
- Later in the day, joint pain and fatigue may return.
- Puffiness of the hands can occur.
- Recurrent attacks of arthritis are experienced by one-third of those with lupus.

- Compared to rheumatoid arthritis, lupus arthritis is less disabling and it usually does not cause severe destruction of the joints. Fewer than 10 percent of people with lupus arthritis will develop deformities of the hands and feet. These are associated with weakening of cartilage and bone and can be seen in the x-ray of the joints. Referred to as "Jaccoud-type deformities," these are reversible conditions.



Diagnosis

The pattern of joint pain and the distribution of the inflamed joints are the best clues in determining whether the joint pain is caused by SLE. X-rays of the painful joints are usually normal in SLE. Fluid removed from a painful joint will show a low-grade inflammation. When arthritis of several joints is the only symptom, establishing the diagnosis of SLE and differentiating it from other types of arthritis can be difficult. Careful observation and re-evaluation by the physician for other symptoms of SLE is essential in making the diagnosis.

- Neither a positive lab test for antinuclear antibodies or for rheumatoid factor in the blood are proof of SLE or rheumatoid arthritis. Both occur in either disease as well as in people with other medical conditions.
- However, a positive test for anti-DNA and/or anti-Sm is more specific for SLE and is helpful in the diagnosis.

Treatment

Proper and early treatment for most forms of arthritis, including SLE and rheumatoid arthritis, is available and can significantly slow down damage to the joints and lessen the pain and stiffness. Lupus arthritis is treated with non-steroidal anti-inflammatory drugs (NSAIDs). These medications are effective for most people and usually are well-tolerated. They include:

- aspirin
- salsalate (saliscylate)
- naproxen
- ibuprofen
- indomethacin

- When NSAIDs are not adequate to control arthritis, antimalarial agents such as hydroxychloroquine (Plaquenil) are added.
- Corticosteroids (prednisone) are used when the joints remain swollen and despite other treatment.
- Immunosuppressive medications can be effective for inflammatory arthritis. However, in general, these agents are not used solely or primarily for lupus arthritis. These drugs include:
  - cyclophosphamide
  - azathioprine
- methotrexate

Fibromyalgia In SLE

Fibromyalgia is a chronic disorder. Its characteristics include:

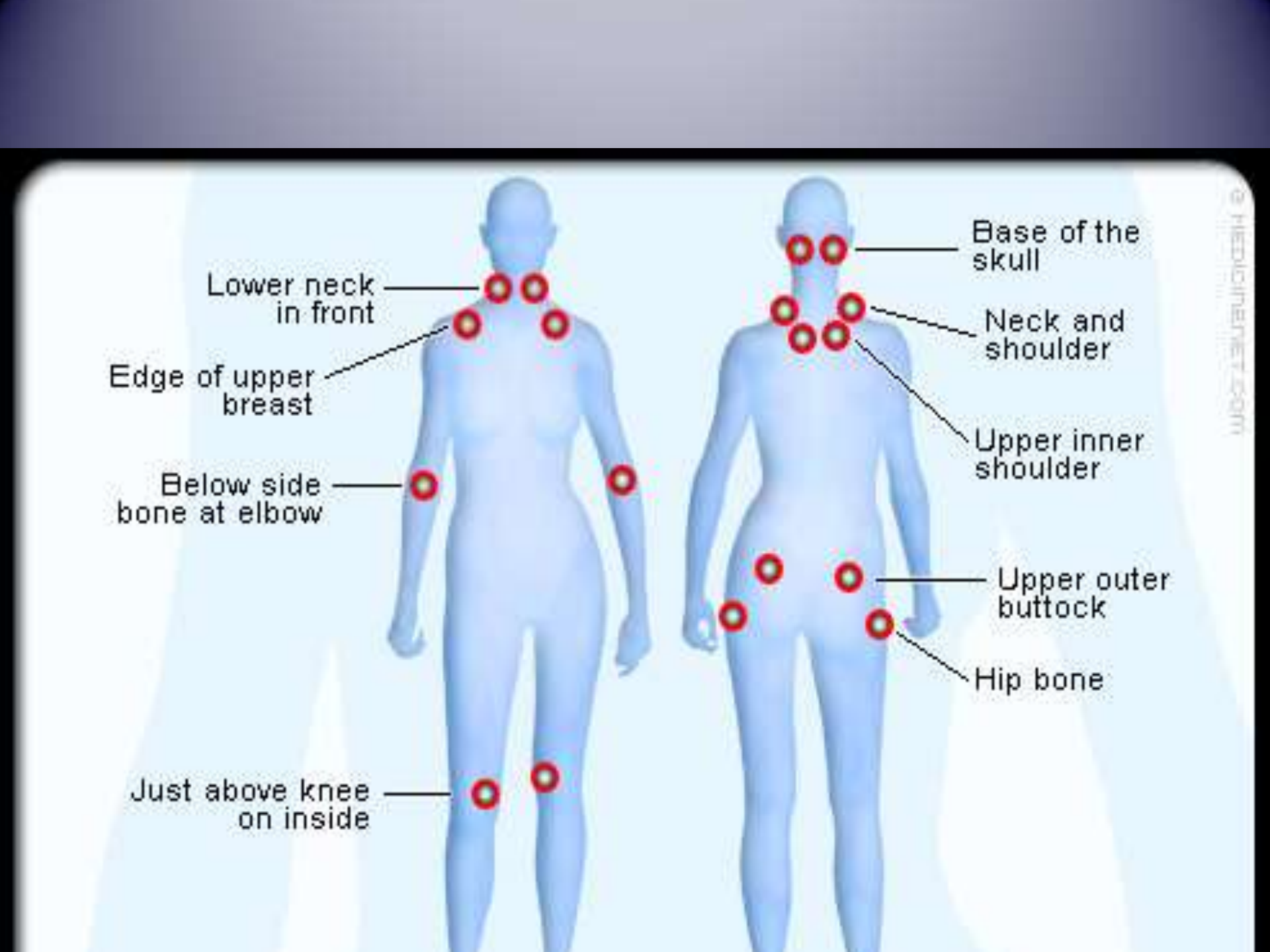
- widespread pain in muscles and joints
- fatigue
- generalized weakness
- non-restful sleep

- Other symptoms of fibromyalgia include:
  - headache
  - changes in mood
  - difficulty in thinking and concentration
  - irritable bowel
  - urinary urgency
- applying pressure to specific locations on the neck, back, chest, and limbs (tender points) will cause pain and tenderness

- points) will cause pain and tenderness.
- Fibromyalgia is estimated to occur in up to 2 percent of the U.S. population.
  Fibromyalgia may exist with other conditions, including SLE and rheumatoid arthritis.
  The cause of fibromyalgia is not known.

  Diagnosis
  The symptoms - such as fatigue, musculoskeletal pain, mood and cognitive abnormalities - may be mistaken for increased disease activity (also called a flare). However, laboratory markers of lupus flare, including a low serum complement level and high levels of anti-DNA antibodies, do not occur in fibromyalgia.

  Treatment
  Fibromyalgia is treated with NSAIDs and other agents to relieve pain.
  Other medications


Lower neck in front
Edge of upper breast
Below side bone at elbow
Just above knee on inside
Base of the skull
Neck and shoulder
Upper inner shoulder
Upper outer buttock
Hip bone

can be used to help get restful sleep. A comprehensive program of aerobic exercise, physical therapy, relaxation techniques, and coping skills is beneficial for many people with this disease.

Avascular Necrosis of the Bone (AVN

Avascular necrosis of the bone - also called aseptic necrosis or osteonecrosis - is characterized by:

- diminished blood flow
- increased pressure within a portion of the bone

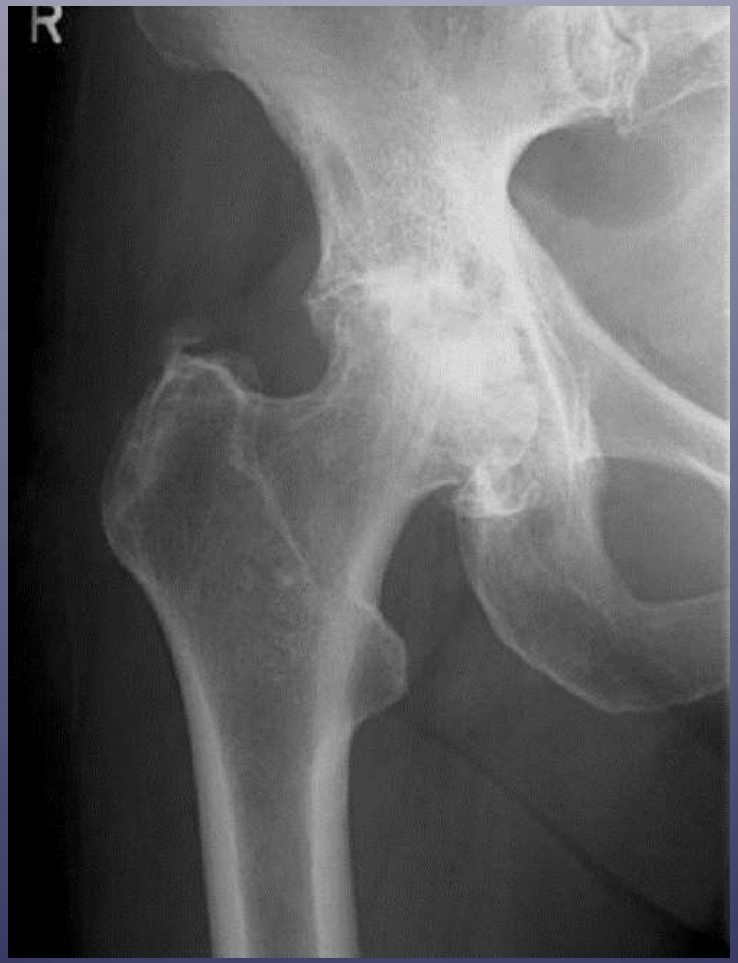
- Diagnosis

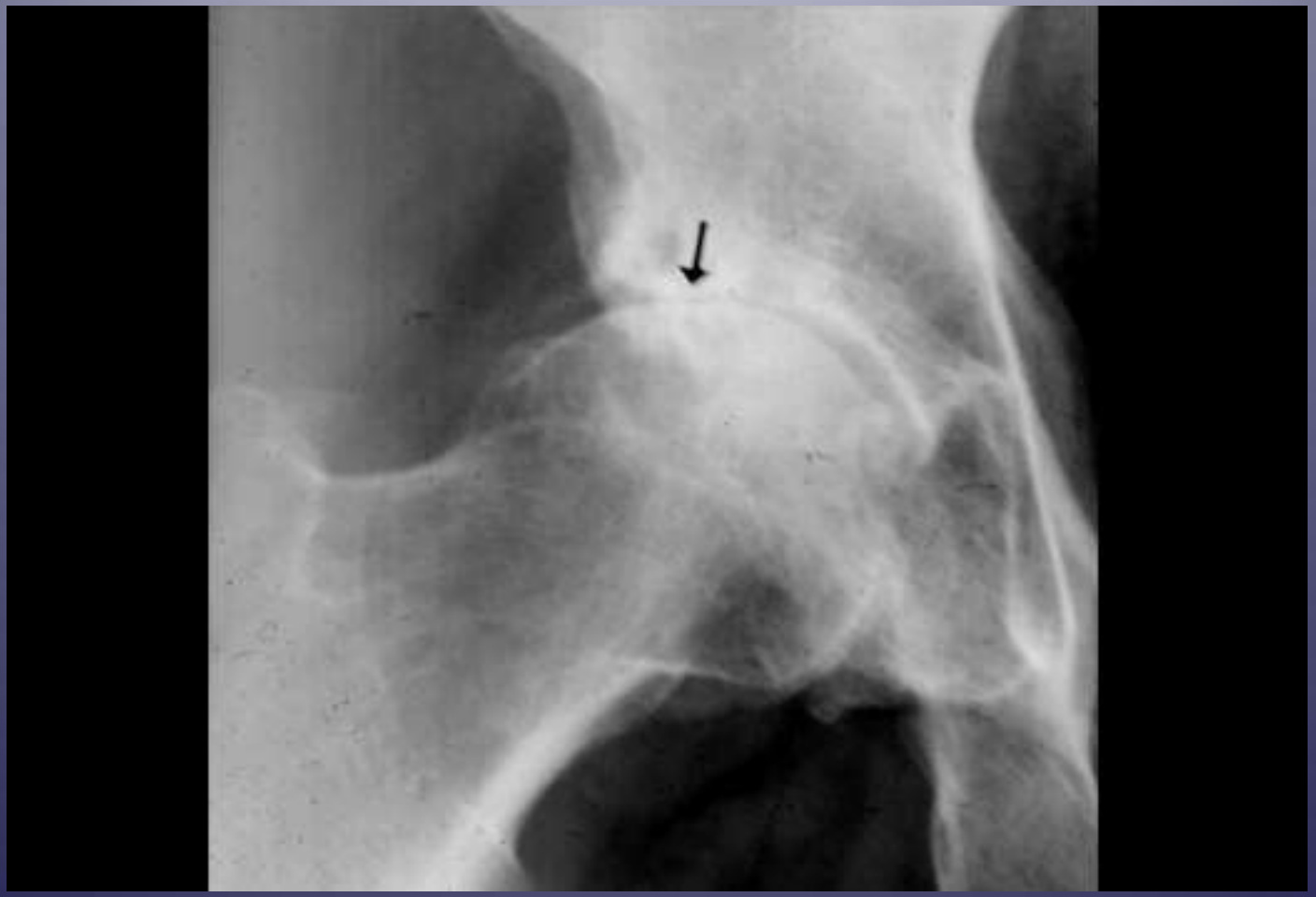
The diagnosis of AVN can be confirmed by magnetic resonance imaging (MRI) scan and/or X-ray of the joint. MRI is a more sensitive test and may be helpful in diagnosing the early stage of AVN. Early diagnosis is important so that steps can be taken to lessen damage to the bone.

The cause of AVN is not known. However, it is associated with several factors:

- prolonged use of high doses of corticosteroids
- alcohol abuse
- sickle cell anemia (an inherited disease)
- pancreatitis
- trauma and other conditions.
-

- **stage I**
  - X-ray : normal or minor osteopaenia
  - MRI : oedema
  - bone scan: increased uptake
  - clinical symptoms: pain typically in the groin
- **stage II**
  - X-ray : mixed osteopaena &/or sclerosis
  - MRI : geographic defect
  - bone scan : increased uptake
  - clinical symptoms: pain and stiffness
- **stage III**
  - X-ray : crescent sign & eventual cortical collapse
  - MRI : same as Xray
  - clinical symptoms : pain and stiffness+/- radiation to knee and limp
- **stage IV**
  - X-ray : end stage with evidence of secondary degenerative change
  - MRI : same as Xray
  - clinical symptoms : pain and limp


R



- There is weakening of the bone which causes tiny breaks, and eventually the bone surface collapses. The hips, shoulders, and knees are most commonly affected. The initial symptom of AVN is pain in these joints, especially on movement and weight-bearing, such as:
  - walking
  - running
  - lifting objects.
- This leads to stiffness, muscle spasm, and limited movement of the affected joint. As the condition becomes more advanced, pain may occur at rest, especially at night

- Treatment

Currently there is no effective medical treatment that can reverse this condition.

- In the early stages of AVN, the person is advised to avoid unnecessary stress to the affected joint, such as prolonged walking and weight-bearing.
- The use of a cane or crutches helps to take weight off the affected extremity.
- NSAIDs and other medications are prescribed to relieve pain.
- In advanced cases of AVN, surgery (including artificial joint replacement) can be effective in relieving pain and improving mobility and function.
- High doses of steroids, taken for an extended period, will increase the risk for development of AVN. Whenever possible, the steroid dose is reduced to lessen the chance of developing this condition.

Lupus Myositis

- Muscle pain (myalgia) and muscle tenderness are common, especially during periods of increased disease activity (flare), and occur in 50 percent of those with SLE.
- Some people develop inflammation of the skeletal muscles (myositis), which causes weakness and loss of strength.
- Lupus myositis commonly involves the muscles of :
  - the neck
  - pelvic girdle and thighs
  - shoulder girdle and upper arms.

- The onset of the weakness can be tricky to detect, but difficulty in climbing stairs and getting up from a chair are early symptoms. Later, there may be difficulty in :
  - lifting objects onto a shelf
  - combing the hair
  - getting out of the bath
  - raising the head
  - turning over in bed.

Diagnosis

- The diagnosis of lupus myositis is confirmed by:

1. elevated levels of certain enzymes (CPK, aldolase, SGPT and SGOT) in the blood
2. certain abnormalities in an electromyogram (EMG) test which measures electrical activity of the muscle fibers.

- Another test that is sometimes used is a biopsy of the thigh or arm muscle. The tissue is examined under the microscope for evidence of inflammation and destruction of muscle fibers.

Treatment

- Corticosteroids (prednisone) are the drug of choice in the treatment of lupus myositis.
- A high dose (50 mg per day of prednisone or equivalent) is given to suppress and control the muscle inflammation.
- Muscle strength will gradually improve and serum enzymes will fall to normal levels.
- With clinical improvement, the dose of prednisone is tapered gradually.
- The vast majority of people with lupus myositis respond promptly to corticosteroid therapy.
- Those few individuals who fail to respond adequately to steroids will be prescribed an immunosuppressive agent such as methotrexate or azathioprine. An exercise program supervised by a physical therapist is helpful in regaining normal muscle strength and function.

Drug-Induced Muscle Weakness

- Muscle weakness can be a side effect of certain medications, including :
  - prednisone and other corticosteroids
  - cholesterol-lowering drugs
  - hydroxychloroquine (Plaquenil).
- Drug-induced muscle disease should be ruled out as a cause of weakness in a person with lupus who is taking any of these medications. Decrease of the corticosteroid dose or discontinuation of the offending agent usually results in an improvement of the muscle strength

The Challenge

- Treat Active Lupus

- Prevent Damage from:
- - Active lupus
- - Corticosteroids
- - Immunosuppressive agents

Treatment of active SLE Organ System Approach

- Use the drug with the:
- - Least side effects
- - Lowest dose to control disease
- - Long term damage prevention

- Mild disease: Avoid Steroids
- Severe disease: Aggressive treatment

Sulfur-Rich Foods

- Sulfur is a mineral necessary for the absorption of calcium that helps your body rebuild bone cells. It may also improve your body's ability to repair connective tissue and cartilage, reversing damage caused by immune cells. Boost your intake of sulfur by consuming foods such as onions, eggs, asparagus, garlic, lentils, cabbage, fish and soybeans.

Antioxidant-Rich Foods

- Foods rich in antioxidants may prevent damage to your muscles, bones and organs. Antioxidants are nutrients that starve free-radical molecules of the oxygen they need to attack and destroy healthy cells. Antioxidants such as vitamin C and vitamin A may also help regulate immune-system function. Antioxidants are found in citrus fruits, kale, spinach, avocados, pomegranates, blueberries, cherries, tomatoes and blackberries.

Essential Fatty Acids

- Essential fatty acids may serve several functions that help relieve symptoms of lupus. Fatty acids may prevent damage to the muscles of your heart, reducing your risk of lupus-related heart disease, and help reduce inflammation in your muscles and joints, relieving pain and stiffness. Essential fatty acids may also reduce your risk of kidney disease, a common complication of lupus. Flaxseeds, fish, walnuts and black currant seed oil contain abundant sources of essential fatty acids.

Foods to Limit or Avoid

Limit your intake of sodium, as well as meats high in saturated fats such as beef, pork, chicken legs and lamb. Sodium and saturated fats increase the workload on your kidneys that may increase your risk of developing lupus-related kidney disease.

Avoid nightshade vegetables such as eggplant, potatoes, tomatoes and peppers. These foods contain a chemical compound called solanine, which may increase joint inflammation and pain. Also, avoid alfalfa sprouts -- these sprouts contain canavanine, a chemical that may be toxic to muscle and connective tissue cells

Systemic Lupus Erythematosus

PROGNOSIS

- Usually chronic, relapsing, and unpredictable. Remissions may last for years.
- If initial acute phase is controlled, even if very severe (with cerebral thrombosis or severe nephritis), the long-term prognosis is usually good.
- The 10-yr survival in most developed countries is > 95%. Improved prognosis is in part due to earlier diagnosis and more effective therapies.
- More severe disease requires more toxic therapies, which increase risk of mortality.

- **Thank you**